

REMARKS

Claim 33-35, 38, 41, 44 and 48 have been amended and claim 47 canceled without prejudice. Support for amendment of the claims are found in the specification as filed. In particular, support for claims 33-35 can be found at page 20, lines 12-23. No new matter is included.

1. **The Objection Is Obviated**

Claims 47 and 48 are objected to under CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. The Examiner asserts that because the claims specifically set forth that the claimed nucleic acids comprise the sequence of "complementary DNA." Applicant respectfully disagrees. In the interest of expediting prosecution, claim 47 is canceled. Claim 48 has been amended to depend only from claim 1 or 41 which do not recite the term "complementary DNA". The objection is obviated.

2. **The Rejection Under 35 U.S.C. § 112, 2nd Paragraph Is Obviated**

Claim 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As suggested by the Examiner, the reference to claims 33-35 and 38 in claim 48 is deleted. The objection is obviated.

3. **The Rejection Under 35 U.S.C. § 112, First Paragraph Is Obviated**

Claims 33-49 are rejected under 35 U.S.C., first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Applicant traverses the rejection on the basis of the claims as amended.

In order to provide an adequate written description, the specification must reasonably convey to the artisan that the inventor had possession at that time of the claimed subject matter. While a patent applicant does not have to describe exactly the subject matter claimed, the description must clearly allow persons of ordinary skill in the art to recognize that the applicant invented what is claimed. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991) (citing In re Gosteli, 872 F.2d 1008, 1012,

10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989)).

The Examiner contends that the possible variations in the structure of the polypeptides encoded by the instantly recited nucleic acids variants is extensive. Allegedly, the language "substantially the entire complement" is indefinite and encompasses situations in which only portions of the fragments hybridize. Applicant disagrees as the term "substantially" is defined in the specification. However, in the interest of expediting prosecution, Applicant has amended claims 33, 34 and 35 to cancel the recitation of "substantially". The amended claims require that the claimed nucleic acid hybridizes to the entire complement of the recited nucleic acids, and thus, eliminating the situation where portions of the nucleic acid hybridize. Applicant points out that the amended claims further impose a size limitation on the nucleotide sequence of the complementary DNA that is at least the same as or greater than that of the recited nucleic acids.

The Examiner further contends that there does not appear to be any requirement that relevant, identifying characteristics of the instant nucleic acids must be shared among members of the genus recited. Neither are there testable functions recited for the polypeptides encoded by these variant nucleic acids sequences to provide some correlation between a particular structure and an associated, testable, function.

In response, Applicant points out that the claims have also been amended to recite that the nucleic acid molecule encodes a polypeptide that is specifically recognized by an antibody that also specifically recognizes a DSCAM having the amino acid sequence of a recited SEQ ID NO:. Support for such polypeptides are found in the specification at page 20, lines 12-23.

According to the Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement (Federal Register v. 66, no. 4, pages 1099-1111, January 5, 2001, the "Guidelines"), the written description requirement may be satisfied by disclosure of relevant, identifying characteristics, i.e., structure or other physical or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See footnote 42 of the Guidelines wherein it is stated that examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length, and also detailed restriction enzyme maps, antibody cross-reactivity, unique cleavage

by particular enzymes. Applicant submits that the claimed genus of nucleic acid molecules share a set of unifying identifiable characteristics (hybridization under stated stringent conditions to recited nucleic acids; a minimum size) and testable communal function (immunospecific binding of antibody to encoded polypeptide), which are fully described in the specification as filed. One of skill in the art would recognize from this combination of characteristics that Applicant has possession of the claimed genus of nucleic acid molecules.

Applicant submits that the variation of the nucleotide sequence of the complementary DNA is governed by the common attribute of hybridizing under defined conditions to nucleic acid molecules of known sequences. In the instant claims, the stated hybridization conditions are highly stringent which reduces the variation among species in the claimed genus. The differences within the claimed genus is further reduced by the minimum size limitation of the complementary DNA. Moreover, the claimed genus of complementary DNA shares a necessary common structural attribute that is correlated to its functional ability to encode a polypeptide that exhibit a readily testable biological property of the neural cell adhesion molecule of the invention. One of ordinary skill in the art would not expect substantial variation among species encompassed within the scope of the amended claims. Weighing all factors including stringent hybridization conditions, minimum size limitation and the encoding of a polypeptide that specifically binds or cross-reacts immunologically with an antibody directed to a DSCAM, taken in view of the level of knowledge and skill in the art, the skilled person would recognize from the disclosure that applicant was in possession of the genus of claimed DNA. Accordingly, the amended claims meet the written description requirements. The rejection of claims 33-35 and dependent claims should thus be withdrawn.

The Examiner proposes that claims 38 and 41 and 45 be amended to indicate that the claimed nucleic acids "consist of" the nucleotide sequence of the encoded polypeptide would overcome the written description rejection. Although Applicant disagrees with the reasoning of the Examiner's rejection and proposal, in the interest of expediting prosecution, claims 38, 41 and 45 have been amended to recite the transition "consisting of".

Claims 33-49 are rejected under 35 U.S.C. 112, first paragraph, for lacking enablement for variants of the nucleic acids of SEQ ID NOS: 1 and 10 which hybridize, subfragments comprising larger nucleotide sequences or which encode subfragments of the polypeptides of SEQ ID NO: 2 or SEQ ID NO: 11, or various oligonucleotides of unspecified length and undefined composition. The Examiner contends that the function of polypeptides

encoded by these "variant" nucleic acid sequences would be highly unpredictable and referred to Attwood (Science 200; 290:471-473), Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39), and Metzler et al. (Nature Structural Biol. 1997; 4:527-531). The Examiner reasoned that the fact that two nucleic acid sequences hybridize under high stringency conditions does not in and of itself require that the two sequences share any functional activity, nor does the presence of a shared subsequence. The Examiner surmised that hybridization language in the absence of a *testable function for the encoded polypeptide* does not allow the skilled artisan to make and use the hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

In response, Applicant submits that the claims at issue have been amended as described above to recite an additional limitation that at least a portion of the nucleotide sequence of the claimed nucleic acid encodes a polypeptide which shares the same or structurally similar antibody binding sites as the DSCAM proteins disclosed in the specification. As the functional properties of the claimed nucleic acids are further defined by the amendment, Applicant submits that one of skill in the art would readily know how to make and test any species of nucleic acids encompassed by the claim without undue experimentation.

In view of the foregoing, Applicant submits that the rejections under section 112, first paragraph is obviated.

4. The Rejection Under 35 U.S.C. § 101 Is In Error

Claims 1 and 31-49 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility. Applicant respectfully disagrees.

According to 35 U.S.C. § 101, whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter may obtain a patent therefor subject to the conditions and requirements of 35 U.S.C. The threshold of utility is not high. *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700, 1702 (Fed. Cir. 1999). An invention is "useful" under 35 U.S.C. § 101 if it is capable of providing some identifiable benefit. *Id.* (citing *Brenner v. Manson*, 383 U.S. 519, 534, 148 USPQ 689, 695 (1966)). An applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility

requirement of 35 U.S.C. 101. See, e.g., *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *In re Irons*, 340 F.2d 974, 144 USPQ 351 (CCPA 1965); *In re Langer*, 503 F.2d 1380, 183 USPQ 288 (CCPA 1974); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (CCPA 1977).

The Examiner contends that the specification does not provide any evidence to support the diagnostic and therapeutic utilities beyond the knowledge that this gene maps to the region of the genome that is associated with Down Syndrome and this gene is a putative cell adhesion molecule. The Examiner asserts that none of these proposed utilities is considered to be a substantial utility because they are all speculative and would require further experimentation to reasonably confirm which, if any, are actual utilities of the instantly disclosed human and mouse molecules. As such, the Examiner contends that these asserted utilities are an invitation for a researcher to further experiment to determine how to utilize the claimed nucleic acid molecules. Applicant respectfully disagrees and points out that the Examiner's characterization of the utilities of the claimed invention as "speculative" indicates that the rejection is apparently based on a lack of credible utility. According to MPEP 2107.02(III)(B):

Office personnel should be careful, however, not to label certain types of inventions as "incredible" or "speculative" as such labels do not provide the correct focus for the evaluation of an assertion of utility. "Incredible utility" is a conclusion, not a starting point for analysis under 35 U.S.C. 101. A conclusion that an asserted utility is incredible can be reached only after the Office has evaluated both the assertion of the applicant regarding utility and any evidentiary basis of that assertion. The Office should be particularly careful not to start with a presumption that an asserted utility is, *per se*, "incredible" and then proceed to base a rejection under 35 U.S.C. 101 on that presumption. (emphasis in original)

Furthermore, according to MPEP 2107.02(IV), it is stated that:

... Whenever possible, the examiner should provide documentary evidence regardless of publication date (e.g., scientific or technical journals, excerpts from treatises or books, or U.S. or foreign patents) to support the factual basis for the *prima facie* showing of no specific and substantial credible utility. If documentary evidence is not available, the examiner should specifically explain the scientific basis for his or her factual conclusions.

Where the asserted utility is not specific or substantial, a *prima facie* showing must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial.

Furthermore, the Examiner's attention is directed to the opinion of the Court of

Appeals for the Federal Circuit (C.A.F.C.) in *In re Brana*, 5 F.3d 1557, 34 U.S.P.Q.2d 1437 (Fed. Cir. 1995). In *In re Brana*, the C.A.F.C. reversed the Board's decision and explained the legal standard for compliance with the relevant § 112 requirement that "unless there is reason to doubt the objective truth of the statements contained [in the specification] which must be relied on for enabling support," a specification's disclosure "must be taken as in compliance with the enabling requirement." *Id.* at 1441 (emphasis in the original).

Here, the Examiner did not submit any evidence to overcome the presumption of truth that the assertion of utility by the applicant enjoys. The Examiner merely concluded generally that the assertions are speculative. The Examiner failed to establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility.

Applicant submits that in view of the disclosures in the specification, it is more likely than not that one of ordinary skill in the art would reasonably correlate DSCAM's structure and expression pattern in fetus and adult animals with a role in DS and associated phenotypes. Indeed, the disclosures in the specification have been published in a peer-reviewed scientific journal, Yamakawa et al., 1998, Human Molecular Genetics, 7:227-237 (see Exhibit A attached hereto). The data presented in the application and Yamakawa et al. support the reasoning used in asserting a utility and the asserted utility of the invention is consistent with knowledge in the art at the time.

In further support, the Examiner's attention is invited to Exhibit B (Barlow et al., 2002, Biochem. Biophys. Res. Comm. 293:881-891), which is a recent peer-reviewed publication by the inventor that reports the role of DSCAM in dorsal-ventral cell fate determination in the embryonic central nervous system, and in neuronal function of the adult cortex and cerebellum. In particular, Applicant points out that the correlation of DSCAM functions and DS phenotypes is further confirmed by the observation that the level of DSCAM expression is increased by more than 20% in the DS brain (see Barlow et al., page 889, under *Mammalian DSCAMs and human disease*; and reference 34¹). Applicant submits that there is no basis for one of skill in the art (including the reviewers of the journals and the two previous examiners assigned to the present application) to doubt the reliability of Applicant's data as provided in the specification. Consequently, the claimed utilities are substantiated by valid observations, which when considered as a whole, will lead a person of

ordinary skill to conclude that the asserted utility is more likely than not true.

The contention that the claimed inventions lack specific utility is untenable. It is Applicant's initial goal to identify genes that are responsible for the phenotypes of Down's Syndrome (DS) which led to the use of direct cDNA selection techniques using bacterial artificial chromosomes containing human chromosome 21 regions from 21q22.2-q22.3 and cDNAs from a trisomy 21 human fetal brain (see specification, Example 2, page 50). The claimed nucleic acids were isolated from a human trisomy 21 fetal brain cDNA library and named Down Syndrome Cell Adhesion Molecules (DSCAM) clones (see specification, Example 3, page 52, and page 53, lines 20-22.) At the outset, it is clear that Applicant's experimentations were expressly directed to finding reagents specifically for the diagnosis and/or treatment of DS and associated phenotypes.

According to MPEP 2107.01(I), under the subsection "*Specific Utility*" (at page 2100-32):

A general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition. Assertions falling within the latter category are sufficient to identify a specific utility for the invention.

Here, Applicant has asserted the utilities of the claimed nucleic acids, which are clearly specific, in the specification as filed. The chromosomal location of DSCAM suggests a role in the DS phenotype as supported by studies of patients with partial trisomy 21 (see specification, page 43 lines 3-19). DSCAM is a member of the immunoglobulin superfamily of cell adhesion molecule (Ig-CAMs) that is known in the art to play central roles in the development and plasticity of human nervous system (see specification, page 7, line 28 to page 8, line 35). Applicant teaches that the timing of DSCAM expression and the specificities of expression in certain neuronal tissues and cells correlates with a role in the pathology of DS phenotypes, e.g., DSCAM overexpression and abnormalities of dendritic structures (see specification, page 10, lines 11-17; page 21, lines 23-26), Hirschsprung's disease (see specification, page 44, lines 2-4), and cognitive defects in DS (see specification, page 8, lines 9-16; page 21, lines 23-26). Applicant's data reasonably indicate such a correlation that is specifically applicable to DS.

¹ Bahn S, Mimmack M, Ryan M, Caldwell MA, Jauniaux E, Starkey M, Svendsen CN, Emson P. , Neuronal target genes of the neuron-restrictive silencer factor in neurospheres derived from fetuses with Down's syndrome: a gene expression study, *Lancet* (2002), 359:310-315.

Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

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Respectfully submitted,

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